IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

Atty Dkt. -47-217

C# M#

WEST et al

TC/A.U. 1649

Serial No. 10/517,653

Examiner: Kolker, D.E.

Filed: March 8, 2005

Date: June 11, 2007

Title: METALLOTHIONEIN BASED NEURONAL THERAPEUTIC AND THERAPEUTIC METHODS

FACSIMILE CERTIFICATE

I hereby certify that this Amendment is being transmitted by facsimile to the Patent and Trademark Office on June 11, 2007, specifically to 571-273-8300.

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Leonard C. Mitchard
Reg. No. 29,009

No. of pages transmitted (including this cover sheet): 5 pages

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

RESPONSE/AMENDMENT/LETTER

This is a response/amendment/letter in the above-identified application and includes an attachment which is hereby incorporated by reference and the signature below serves as the signature to the attachment in the absence of any other signature thereon.

☐ **Correspondence Address Indication Form Attached.**

Fees are attached as calculated below:

Total effective claims after amendment 0 previously paid for 20	(at least 20) =	0 minus highest number x $50.00	$0.00 (1202)/$0.00 (2202)	$
Independent claims after amendment 0 previously paid for 3	(at least 3) =	0 minus highest number x $200.00	$0.00 (1201)/$0.00 (2201)	$
If proper multiple dependent claims now added for first time, (ignore improper); add			$360.00 (1203)/$180.00 (2203)	$
Petition is hereby made to extend the current due date so as to cover the filing date of this paper and attachment(s)			One Month Extension $120.00 (1251)/$60.00 (2251) Two Month Extensions $450.00 (1252)/$225.00 (2252) Three Month Extensions $1020.00 (1253/$510.00 (2253) Four Month Extensions $1590.00 (1254/$795.00 (2254) Five Month Extensions $2160.00 (1255/$1080.00 (2255)	$
Terminal disclaimer enclosed, add			$130.00 (1814)/ $65.00 (2814)	$

☐ Applicant claims "small entity" status. ☐ Statement filed herewith

Rule 56 Information Disclosure Statement Filing Fee	$180.00 (1806)	$	0.00
Assignment Recording Fee	$40.00 (8021)	$	0.00
Other:		$	0.00
	TOTAL FEE	$	0.00

☐ **CREDIT CARD PAYMENT FORM ATTACHED.**

The Commissioner is hereby authorized to charge any deficiency, or credit any overpayment, in the fee(s) filed, or asserted to be filed, or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Account No. 14-1140. A duplicate copy of this sheet is attached.

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

WEST et al — Atty. Ref.: 47-217; Confirmation No. 5626

Appl. No. 10/517,653 — TC/A.U. 1649

Filed: March 8, 2005 — Examiner: Kolker, D.E.

For: METALLOTHIONEIN BASED NEURONAL THERAPEUTIC AND THERAPEUTIC METHODS

* * * * * * * * * * * *

June 11, 2007

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

RESPONSE

In response to the restriction requirement mailed April 11, 2007, Applicants hereby elect Group 1. The election is made with traverse.

The Action cites Ebadi in support of the requirement. However, in Ebadi, metallothionein was **never** administered to either cultured neurones or to animals. All the experimental data and disclosures in Ebadi refer to the induction of endogenous metallothionein secondary to administration of another agent in animals. The thrust of Ebadi was to look for enhanced neuronal survival, **not** regenerative growth.

The present invention is not concerned with the action of metallothionein on other cell types, both neutral or otherwise, which might contribute to the regenerative effects seen in animals. Such regenerative effects seen in animals in other experimental work

cannot contribute or provide any teachings to the results of the current invention obtained in culture. Nor is the present invention concerned with the actions of injured neurones and other cell types after injury.

Ebadi examines the effect of a compound with putative protective effects, selegiline, on the survival and morphology of dopaminergic neurons in animals and in cell culture. Ebadi presents several sets of results which involve metallothionein.

1. Table 1. shows that metallothionein levels decrease in the striatum of the rat brain following treatment with 6-OHDA (a well known toxin of neurons in this region). This finding has no relevance to the current invention.

2. Table 2. demonstrates the free radical scavenging abilities of MT-I and MT-II. This finding also has no relevance to the current invention.

3. Figure 3. treatment of rats with the toxin 6-OHDA, and some animals are pre-treated with selegiline, or bis(thisemicarbaxone), an agent believed to induce metallothionein in the brain. Loss of striatal neurons is measured as a consequence of this treatment (this is not the same as administering metallothionein and it does not constitute evidence of an effect of metallothionein, which may or may not exist in this model).

The following points are evident:

(a) Ebadi makes **no report** of administering metallothionein, either to animals or to neuronal cultures. The administration of exogenous MT is a key feature of the invention.

(b) Ebadi makes **no finding** about the ability (or otherwise) of metallothionein to affect the regenerative growth of neurons.

(c:) Ebadi does **not** investigate the interaction of metallothionein and neurons, either in culture or in animals.

The Action states that the paper discloses "contacting neurons with solutions comprising MT-II protein and protecting the neurons from damage (see for example p. 107 last paragraph of the results section, and Table II)". This is not correct. Ebadi does not describe applying metallothionein (any isoform) to neurons. Therefore, discussion about the relative effects of MT-I and MT-II in this context are **not relevant,** since the efficacy of either on neuronal regenerative growth was not investigated.

In contrast to Ebadi, the experimental data pertaining to the present invention has demonstrated:

1. Metallothionein increases regenerative neuronal growth when applied to i) immature and ii) mature cortical neurons in culture.

2. Non-neuronal cell types are not necessary for the regenerative effect of metallothionein on neurons to be observed.

3. Metallothionein likewise increases regenerative neuronal growth when applied to cortical lesions in animals.

Based on the above, it is believed that Ebadi is not relevant to the currently claimed invention. Withdrawal of the restriction requirement and examination of all claims on the merits are respectfully requested.

WEST et al
Appl. No. 10/517,653
June 11, 2007

Respectfully submitted,

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